Early activation of the interleukin-23-17 axis in a murine model of oropharyngeal candidiasis

Type:

Article

Abstract:

P>Candida albicans is an oral commensal yeast that causes oropharyngeal candidiasis (OPC) in immunocompromised individuals. The immunological pathways involved in OPC have been revisited after the interleukin-17 (IL-17) pathway was implicated in fungal immunity. We studied immediate (< 24 h) and adaptive (3-6 day) IL-12 and IL-23-17 pathway activation in naive p40-/- mice, which lack IL-12 and IL-23 and develop severe, chronic OPC upon oral inoculation with C. albicans. Macrophages from p40-/- mice were less efficient than C57BL/6J controls at killing C. albicans in vitro but very low numbers in the oral mucosae of infected C57BL/6J mice suggest that they are not critical in vivo, at least in this strain. Migration of macrophages to regional lymph nodes of infected p40-/- mice was impaired; however, dendritic cell migration was not affected. Recombinant IL-12 therapy provided only temporary relief from OPC, suggesting that IL-23 is required for full protection. In C57BL/6J mice, but not p40-/- mice, messenger RNAs encoding IL-23p19 and IL-17 were induced in the oral mucosa within 24 h of infection (6 +/- 0.6 and 12 +/- 2.7-fold). By day 6 of infection in C57BL/6J mice, IL-17A messenger RNA level had increased 5.1 +/- 1.8 and 83 +/- 21-fold in regional lymph nodes and oral tissues respectively. Ablation of p40 was associated with delayed or abrogated induction of IL-17A pathway targets (monocyte chemoattractant protein-1, IL-6 and macrophage inflammatory protein-2), and a lack of organized recruitment of neutrophils to the infected oral mucosa. Overall our data show that the IL-23-17A axis is activated early in the oral mucosae of immunologically naive mice with OPC.

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